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NEWS 19 SEP 26 GEOREF and ENCOMPLIT databases were reloaded on September 24, 2011.

NEWS 20 SEP 26 Updates to the IFIPAT/IFIUDB/IFICDB databases have resumed.

NEWS 21 SEP 26 ECLA Thesaurus in CA/Cplus Improves Patent Searching on STN

NEWS 22 SEP 26 Access AUPATFULL and CANPATFULL databases with STN Viewer

NEWS 23 OCT 26 New STN Revolutionizes Patent Searching for Professionals

NEWS 24 DEC 1 CA/Cplus Now Includes Examiner Citations for Japanese Patents

NEWS 25 DEC 1 CAS Expands Global Patent Coverage - Intellectual Property Corporation of Malaysia Becomes 62nd Authority on CA/Cplus

NEWS 26 DEC 5 STN on the Web Enhancements Include Compatibility with Microsoft Windows 7

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AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2011.

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=> fil medline biosis capplus scisearch embase wpids
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 0.24 0.24

FILE 'MEDLINE' ENTERED AT 16:16:39 ON 04 JAN 2012

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FILE 'WPIDS' ENTERED AT 16:16:39 ON 04 JAN 2012
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=> s hairpin(L)ligase
L1          833 HAIRPIN(L) LIGASE

=> s hairpin(L)ligase(L) (adapter or connector)
L2          17 HAIRPIN(L) LIGASE(L) ADAPTER OR CONNECTOR
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=> dup rem  
ENTER L# LIST OR (END):12  
PROCESSING COMPLETED FOR L2  
L3          13 DUP REM L2 (4 DUPLICATES REMOVED)
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=> d ibib abs 1

L3 ANSWER 1 OF 13 MEDLINE ® on STN DUPLICATE 1
ACCESSION NUMBER: 2011850744 MEDLINE
DOCUMENT NUMBER: PubMed ID: 21876038
TITLE: TLR regulation of SPSB1 controls inducible nitric oxide synthase induction.
AUTHOR: Lewis Rowena S; Kolesnik Tatiana B; Kuang Zhihe; D'Cruz

Akshay A; Blewitt Marnie E; Masters Seth L; Low Andrew;
Willson Tracy; Norton Raymond S; Nicholson Sandra E
CORPORATE SOURCE: Walter and Eliza Hall Institute of Medical Research,
Parkville, Victoria 3052, Australia.
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2011 Oct 1)
Vol. 187, No. 7, pp. 3798-805. Electronic Publication:
2011-08-29.
Journal code: 2985117R. E-ISSN: 1550-6606. L-ISSN:
0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 201111
ENTRY DATE: Entered STN: 22 Sep 2011
Last Updated on STN: 16 Dec 2011
Entered Medline: 22 Nov 2011

AB The mammalian innate immune system has evolved to recognize foreign molecules derived from pathogens via the TLRs. TLR3 and TLR4 can signal via the TIR domain-containing adapter inducing IFN- β (TRIF), which results in the transcription of a small array of genes, including IFN- β . Inducible NO synthase (iNOS), which catalyzes the production of NO, is induced by a range of stimuli, including cytokines and microbes. NO is a potent source of reactive nitrogen species that play an important role in killing intracellular pathogens and forms a crucial component of host defense. We have recently identified iNOS as a target of the mammalian SPSB2 protein. The SOCS box is a peptide motif, which, in conjunction with elongins B and C, recruits cullin-5 and Rbx-2 to form an active E3 ubiquitin ligase complex. In this study, we show that SPSB1 is the only SPSB family member to be regulated by the same TLR pathways that induce iNOS expression and characterize the interaction between SPSB1 and iNOS. Through the use of SPSB1 transgenic mouse macrophages and short hairpin RNA knockdown of SPSB1, we show that SPSB1 controls both the induction of iNOS and the subsequent production of NO downstream of TLR3 and TLR4. Further, we demonstrate that regulation of iNOS by SPSB1 is dependent on the proteasome. These results suggest that SPSB1 acts through a negative feedback loop that, together with SPSB2, controls the extent of iNOS induction and NO production.

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(FILE 'HOME' ENTERED AT 16:16:01 ON 04 JAN 2012)

FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH, EMBASE, WPIDS' ENTERED AT
16:16:39 ON 04 JAN 2012

L1 833 S HAIRPIN(L)LIGASE
L2 17 S HAIRPIN(L)LIGASE(L) (ADAPTER OR CONNECTOR)
L3 13 DUP REM L2 (4 DUPLICATES REMOVED)

=> s l3 and py<=2003
L4 6 L3 AND PY<=2003

=> d ibib abs 1-6

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2012 ACS on STN
ACCESSION NUMBER: 1992:36605 CAPLUS
DOCUMENT NUMBER: 116:36605
ORIGINAL REFERENCE NO.: 116:6161a,6164a
TITLE: Modifying specificities of restriction enzymes
AUTHOR(S): Szybalski, Waclaw

CORPORATE SOURCE: McArdle Lab. Cancer Res., Univ. Wisconsin, Madison, WI, 53706, USA
SOURCE: Biotechnol.: Bridging Res. Appl., Proc. U.S.-Isr. Res. Conf. Adv. Appl. Biotechnol. (1991), Meeting Date 1990, 371-6. Editor(s): Kamely, Daphne; Chakrabarty, Ananda M.; Kornguth, Steven E. Kluwer: Boston, Mass.

DOCUMENT TYPE: Conference; General Review
LANGUAGE: English

AB A review with 12 refs. Using restriction enzymes, modification methyltransferases, single-strand-specific nucleases, ligases, oligo hairpin adapters, and DNA-binding proteins, the authors have designed various strategies for very specific cleavage of small, medium, and very large DNA mol., for detecting point mutations or other genetic changes, for a very efficient printing reaction to produce tetranucleotides, as a highly amplified detection signal, or to synthesize copious amts. of longer sequences, for development of trimming, gene-fusion, or amplification plasmids, and for various other applications, some already tested and some in various stages of development.

L4 ANSWER 2 OF 6 WPIDS COPYRIGHT 2012 THOMSON REUTERS on STN
ACCESSION NUMBER: 2003-021218 [200302] WPIDS
DOC. NO. CPI: C2003-005375 [200302]
TITLE: Selectively amplifying unknown DNA sequence, useful when analyzing single nucleotide polymorphism, by digesting DNA into fragments with single-strand cohesive ends, ligating fragments with a hairpin loop adapter and amplifying the fragments
DERWENT CLASS: B04; D16
INVENTOR: JEON J; JEONG J T; JOUNG I; JUN J T; JUNG I S; LEE J W; PARK H; PARK H O; RHEE J; SONG S; SONG S N; WEON S; WEON S Y; WON S Y; JOUNG I S; RHEE J W
PATENT ASSIGNEE: (BION-N) BIONEER CORP; (BION-N) BIONIA JH; (JEON-I) JEON J; (JOUNG-I) JOUNG I; (PARK-I) PARK H O; (RHEE-I) RHEE J; (SONG-I) SONG S; (WEON-I) WEON S
COUNTRY COUNT: 30

PATENT INFO ABBR.:

| PATENT NO | KIND DATE | WEEK | LA | PG | MAIN IPC | |
|----------------|-----------------------|------|-------|----|----------|-----|
| EP 1256630 | A2 20021113 (200302)* | EN | 10[4] | | <-- | <-- |
| US 20020192769 | A1 20021219 (200315)† | EN | | | <-- | <-- |
| CA 2344599 | A1 20021107 (200316)† | EN | | | <-- | <-- |
| JP 2003009864 | A 20030114 (200316) | JA | 6 | | <-- | <-- |
| KR 2002085727 | A 20021116 (200320) | KO | | | <-- | <-- |
| US 6849404 | B2 20050201 (200511)† | EN | | | <-- | <-- |
| KR 758610 | B1 20070913 (200839) | KO | | | | |
| EP 1256630 | B1 20080618 (200841) | EN | | | | |
| DE 60227130 | E 20080731 (200853) | DE | | | | |
| JP 4435463 | B2 20100317 (201020) | JA | 8 | | | |
| CA 2344599 | C 20110712 (201149)† | EN | | | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|-----------|------|-------------|------|
|-----------|------|-------------|------|

| | |
|-------------------|---------------------------|
| EP 1256630 A2 | EP 2002-10053 20020506 |
| CA 2344599 A1 | CA 2001-2344599 20010507 |
| KR 2002085727 A | KR 2001-25637 20010507 |
| KR 758610 B1 | KR 2001-25637 20010507 |
| US 20020192769 A1 | US 2001-849597 20010507 |
| US 6849404 B2 | US 2001-849597 20010507 |
| DE 60227130 E | DE 2002-60227130 20020506 |
| DE 60227130 E | EP 2002-10053 20020506 |
| JP 2003009864 A | JP 2002-131307 20020507 |
| JP 4435463 B2 | JP 2002-131307 20020507 |
| CA 2344599 C | CA 2001-2344599 20010507 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|---------------|-----------------|
| DE 60227130 E | Based on | EP 1256630 A |
| KR 758610 B1 | Previous Publ | KR 2002085727 A |
| JP 4435463 B2 | Previous Publ | JP 2003009864 A |

PRIORITY APPLN. INFO: KR 2001-25637
 US 2001-849597
 CA 2001-2344599

AN 2003-021218 [200302] WIIDS
 AB EP 1256630 A2 UPAB: 20100323

NOVELTY - A process for selective amplifying DNA of which base sequence is completely unknown, comprising digesting DNA into fragments having a single-strand cohesive end group, ligating the DNA fragments with a hairpin loop adapter having a single-strand cohesive end which can be complementarily combined and ligated on both ends of the DNA, and amplifying the fragments using DNA polymerase and primer.

DETAILED DESCRIPTION - A process (M1) for selective amplifying DNA of which base sequence is completely unknown, comprising:

(a) a step for digesting DNA into fragments which has a single-strand cohesive end group by using restriction enzyme, and separately from the above step, a step for preparing hairpin loop adaptor which has the single-strand cohesive end which can be complementarily combined and ligated on the both ends of the DNA fragments obtained in the above;

(b) a step for ligating the DNA fragments with the hairpin loop adapter thus prepared by using DNA ligase;

(c) a step for removing DNA fragments and hairpin loop adapter which have not participated in the ligation reaction by using exonuclease; and

(d) a step for amplifying the DNA fragment by using DNA polymerase and primer which can combine complementarily on the residual sequence from the adapter.

INDEPENDENT CLAIMS are included for the following:

(1) a process for making library of DNA fragment of which terminal sequence are known by using DNA of which base sequence is completely unknown, comprising:

(a) a step for digesting DNA into fragments which have single-strand cohesive end by using restriction enzyme, and separately from the above, for preparing a series of hairpin loop adapters which have single-strand cohesive end of which base sequence is known;

(b) a step for ligating the DNA fragments with the hairpin loop adapters prepared in the above step (a) by using DNA ligase; and

(c) a step for eliminating the hairpin loop only from the DNA fragments which contain hairpin loop adapter, obtained in step (b) by treating alkaline solution, RNase of single strand specific exonuclease, and

(2) a series of hairpin loop adapters which have single-strand

cohesive ends, where the single-strand cohesive ends are composed of all sorts of single-strand DNA which can be made by random combination of four nucleotides.

USE - The process is useful for analyzing single nucleotide polymorphism in the nucleotide sequences of each individual.

L4 ANSWER 3 OF 6 WPIDS COPYRIGHT 2012 THOMSON REUTERS on STN
ACCESSION NUMBER: 2002-617299 [200266] WPIDS
CROSS REFERENCE: 2001-040475; 2001-366407; 2002-048724
DOC. NO. CPI: C2002-174481 [200266]
TITLE: Isolating DNA containing fragments nicked by Escherichia coli methyl-directed mismatch repair system employs a modified rolling circle amplification procedure which utilizes DNA polymerase III
DERWENT CLASS: B04; D16
INVENTOR: LASKEN R; WEISSMAN S
PATENT ASSIGNEE: (LASK-I) LASKEN R; (MOLE-N) MOLECULAR STAGING INC; (UYYA-C) UNIV YALE; (WEIS-I) WEISSMAN S
COUNTRY COUNT: 1

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|----------------|------|----------|-----------|----|-------|----------|
| US 20020076704 | A1 | 20020620 | (200266)* | EN | 19[5] | <-- |
| US 6576448 | B2 | 20030610 | (200340) | EN | | <-- |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|----------------|----------------|-----------------|----------|
| US 20020076704 | A1 Provisional | US 1998-100996P | 19980918 |
| US 20020076704 | A1 Div Ex | US 1999-398216 | 19990917 |
| US 20020076704 | A1 | US 2001-818927 | 20010328 |
| US 6576448 | B2 Provisional | US 1998-100996P | 19980918 |
| US 6576448 | B2 Div Ex | US 1999-398216 | 19990917 |
| US 6576448 | B2 | US 2001-818927 | 20010328 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|--------|--------------|
| US 6576448 B2 | Div ex | US 6235502 B |

PRIORITY APPLN. INFO: US 2001-818927 20010328
US 1998-100996P 19980918
US 1999-398216 19990917

AN 2002-617299 [200266] WPIDS
CR 2001-040475; 2001-366407; 2002-048724
AB US 20020076704 A1 UPAB: 20060120

NOVELTY - Mismatched DNA containing fragments nicked by MutSLH from two DNA samples are isolated by a modified rolling circle amplification (RCA) method. DNA sample is digested with restriction enzyme, the fragments ligated to Y-shaped adapters forming adapter-fragment constructs which are subjected to nicking by MutSLH proteins and nicked fragments are treated with DNA polymerase(s) to elongate the 3' end.

DETAILED DESCRIPTION - Isolating (M1) mismatched DNA containing fragments nicked by MutSLH (a combination of the three proteins of the Escherichia coli methyl-directed mismatch repair system, collectively called MutSLH) from two DNA samples, comprises:

(a) digesting a first DNA sample with a restriction enzyme to

obtain DNA fragments;

- (b) ligating Y-shaped adapters to the fragments to obtain fragment-plus-adapter constructs;
- (c) repeating the above steps with a second sample;.
- (d) methylating the products formed from (c) of the first sample but not the second sample;
- (e) mixing the methylated and unmethylated products obtained from the samples, denaturing and reannealing to form hemimethylated hetero hybrids;

- (f) treating the fragments produced in step (e) with a MutSLH preparation to nick DNA containing mismatches and form a 3'-OH end; and
- (g) elongating the 3'-OH end with one or more DNA polymerases.

The method can also be carried out by ligating adapters to DNA fragments to obtain fragment-adapter constructs that have a single-stranded (ss) overhang on the 5'-ends and recessed 3'-ends, where the adapters are blocked with a dideoxynucleotide or other modification that prevents the elongation by a DNA polymerase, carrying out (c)-(e) as above, blocking pre-existing nicks on the fragments with dideoxynucleoside triphosphates or their analogs, treating the fragments with MutSLH preparation to form 3'-OH ends and elongating the 3'-OH ends with a DNA polymerase having strand displacement or nick translation capacity.

INDEPENDENT CLAIMS are also included for the following:

- (1) amplifying (M2) DNA using RCA in a manner that results in approximately equimolar amplification of DNA, by amplifying a circle DNA molecule which comprises a stem-and-loop, or a circle DNA molecule containing a universal base, an abasic residue, or other residue that alters the rate of circle replication, where elongation of the circle by a replicating polymerase carrying out the amplification is inhibited;

- (2) a method (M3) for using RCA to obtain approximately equimolar amplification of DNA fragment mixtures by introducing one pause site in a DNA circle, comprises:

- (a) placing within the circle a stretch of one or more abasic sites, a region of high secondary structure and a ligand binding site, and carrying out RCA under conditions such that the pause site slows the DNA polymerase replicating the circle and tends to equalize the number of times the polymerase copies circles of different length; or

- (b) circularizing double stranded DNA (dsDNA) fragments around an adapter such that one strand of the adapter has an internal pause and the outer strand is blocked from ligation at one or both ends; or

- (c) using a splint that has an internal double stranded (ds) segment containing a pause site on one DNA strand, and which has single stranded extensions at both ends complementary to the ends of the single-stranded fragment to be amplified;

- (3) a method (M4) in which fragments of DNA may be circularized and amplified, by cutting DNA with a restriction enzyme that produces a single fragment containing all the markers of the region having pause to be determined, or using the RecA-assisted restriction endonuclease (RARE) method or its variants to produce such a fragment, ligating the cut DNA around an adapter and amplifying the fragment using RCA to obtain a single stranded DNA (ssDNA) from the desired fragment;

- (4) amplifying (M5) segments of a DNA target by RCA, by annealing a padlock DNA that creates a gap comprising the sequence to be amplified, extending the 3'-OH of the padlock DNA with a DNA polymerase which generates a nick, ligating the nick to form a circle DNA, annealing an RCA primer to the circle DNA and carrying out RCA with DNA polymerase III;

- (5) a method (M6) in which large fragments of DNA may be circularized and amplified, by providing a DNA-adapter construct which has a DNA fragment ligated around an adapter that has an internal gap and 5' region of non-complementarity and amplifying the DNA-adapter construct using DNA pol III in a RCA;

- (6) a method (M7) of ligating adapters onto ends of DNA fragments for use in RCA of the DNA, by ligating restriction endonuclease fragments

with an oligonucleotide adapter that forms a hairpin structure with itself such that 3' and 5' ends of the adapter are annealed together and form a proper overhang or blunt end for ligation to the restriction endonuclease fragments, where a circular construct is formed, annealing an oligonucleotide primer to the single-stranded loop portion of the adapters and extending the oligonucleotide primer with a DNA polymerase in RCA reaction; and

(7) a method of carrying out RCA reaction, where at least two different DNA polymerases are employed, one or more of which contains a 3' to 5' exonuclease activity capable of correcting nucleotide misincorporations.

USE - (M1) is useful for isolating mismatched DNA containing fragments nicked by MutSLH from two DNA samples. The procedure is useful for polymorphism analysis (claimed).

The procedure allows for the MutSLH nicking of DNA fragments containing mismatched bases to analyze polymorphism between DNA samples. The methods are useful in phase determination, polymorphism analyses, mismatch scanning procedures and cloning procedures, diagnostics, genotyping, genomic mapping, DNA sequencing and synthesis of DNA probes.

ADVANTAGE - DNA polymerase III holoenzyme provides a superior rate of DNA synthesis and also high processivity which allows rapid replication through regions of high GC content, hair-pin structures, and other regions of secondary structure and regions that normally slow replication due to local sequence context effects.

L4 ANSWER 4 OF 6 WPIDS COPYRIGHT 2012 THOMSON REUTERS on STN
ACCESSION NUMBER: 2002-106604 [200214] WPIDS
DOC. NO. CPI: C2002-032857 [200214]
TITLE: Simultaneous sequence-specific identification and separation of polynucleotide fragments, comprises using restriction endonucleases that recognize degenerate bases in their recognition/cleavage sequence, useful in DNA fingerprinting
DERWENT CLASS: B04; D16
INVENTOR: LI B; LI B Y T M R I; SHI L; SHI L T M R I; WANG X; WANG X T M R I; LI B Y
PATENT ASSIGNEE: (LIBB-I) LI B; (SHIL-I) SHI L; (SYGN-C) SYNGENTA PARTICIPATIONS AG; (WANG-I) WANG X
COUNTRY COUNT: 95

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC | |
|----------------|------|----------|-----------|----|-------|----------|-----|
| WO 2002002805 | A2 | 20020110 | (200214)* | EN | 76[0] | <-- | <-- |
| AU 2001079704 | A | 20020114 | (200237) | EN | | <-- | <-- |
| US 20030148276 | A1 | 20030807 | (200358) | EN | | <-- | <-- |
| US 20030165923 | A1 | 20030904 | (200359) | EN | | <-- | <-- |
| EP 1356096 | A2 | 20031029 | (200379) | EN | | <-- | <-- |
| AU 2001279704 | B2 | 20051215 | (200654) | EN | | | |
| US 7202022 | B2 | 20070410 | (200726) | EN | | | |
| US 7300751 | B2 | 20071127 | (200780) | EN | | | |
| CA 2413423 | C | 20110111 | (201119) | EN | | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|-----------|------|-------------|------|
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| | |
|-------------------------------|--------------------------|
| WO 2002002805 A2 | WO 2001-EP7469 20010629 |
| US 20030148276 A1 Provisional | US 2000-215596P 20000630 |
| US 20030165923 A1 Provisional | US 2000-215596P 20000630 |
| US 7202022 B2 Provisional | US 2000-215596P 20000630 |
| US 7300751 B2 Provisional | US 2000-215596P 20000630 |
| AU 2001079704 A | AU 2001-79704 20010629 |
| AU 2001279704 B2 | AU 2001-279704 20010629 |
| EP 1356096 A2 | EP 2001-957906 20010629 |
| US 20030148276 A1 | US 2001-896324 20010629 |
| US 20030165923 A1 CIP of | US 2001-896324 20010629 |
| US 7202022 B2 | US 2001-896324 20010629 |
| US 7300751 B2 CIP of | US 2001-896324 20010629 |
| EP 1356096 A2 | WO 2001-EP7469 20010629 |
| US 20030165923 A1 | US 2002-236363 20020906 |
| US 7300751 B2 | US 2002-236363 20020906 |
| CA 2413423 C | CA 2001-2413423 20010629 |
| CA 2413423 C PCT Application | WO 2001-EP7469 20010629 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|------------------|----------|-----------------|
| AU 2001079704 A | Based on | WO 2002002805 A |
| EP 1356096 A2 | Based on | WO 2002002805 A |
| AU 2001279704 B2 | Based on | WO 2002002805 A |
| CA 2413423 C | Based on | WO 2002002805 A |

PRIORITY APPLN. INFO: US 2000-215596P 20000630
 US 2001-896324 20010629
 US 2002-236363 20020906

AN 2002-106604 [200214] WIDS
 AB WO 2002002805 A2 UPAB: 20110321

NOVELTY - A new method (M1) for the simultaneous sequence-specific identification and separation of polynucleotide fragments in a polynucleotide population (P1) comprises using restriction endonucleases that recognize degenerate bases in their recognition or cleavage sequence to produce P1 from transcribed RNA. The fragments are then ligated and amplified.

DETAILED DESCRIPTION - A new method (M1) for the simultaneous sequence-specific identification and separation of polynucleotide fragments in a polynucleotide population (P1) comprises using restriction endonucleases that recognize degenerate bases in their recognition or cleavage sequence to produce P1 from transcribed RNA. The fragments are then ligated and amplified.

In detail, M1 comprises:

(a) reverse transcribing an RNA population to provide P1;
 (b) digesting P1 with one or more restriction endonucleases (RE1) having a degenerate recognition or cleavage sequence comprising a degenerate base, where the degenerate base is represented by the formula of N_m , where N is the extent of degeneracy, and m is the number of degenerate bases, to produce restriction fragments having N_m different single-stranded overhangs for each restriction endonuclease;

(c) ligating the restriction fragments having the same overhangs to a series of adapters whose sequences are complementary to the overhangs; and

(d) amplifying the restriction fragments.

INDEPENDENT CLAIMS are included for the following:

(1) a method (M2) for detecting polymorphism comprising:

(a) reverse transcribing an RNA population to provide a polynucleotide population;
 (b) digesting the polynucleotide population with one or more RE1;
 (c) ligating the restriction fragments having the same overhangs to

- a series of adapters whose sequences are complementary to the overhangs;
- (d) amplifying the restriction fragments;
 - (e) sequencing the amplified restriction fragments; and
 - (f) comparing the sequence of the amplified restriction fragments with the sequence of the same polynucleotide from a different source;
- (2) a method (M3) for screening for interactions between a preselected protein and polypeptide fragments, comprising culturing the recombinant host cells of (1) under conditions which enable expression of correctly inserted restriction fragments by the host cell, and assaying the interaction of the polypeptide fragments encoded by the restriction fragments with the preselected protein;
- (3) a method (M4) for detecting a change in the pattern of RNA expression in a tissue or cell associated with an internal or external factor comprising:
- (a) determining the pattern of RNA expression in a first tissue or cell sample not subject to the internal or external change by a method comprising:
 - (i) reverse transcribing an RNA population to provide the polynucleotide population;
 - (ii) digesting a double-stranded cDNA library prepared from the RNA isolated from the first sample with one or more REI, where m is 1-5;
 - (iii) ligating the restriction fragments produced from (ii) having the same overhangs to a series of adapters whose sequences are complementary to the overhangs;
 - (iv) amplifying the restriction fragments; and
 - (v) displaying the pattern of RNA expression in the first sample;
- (b) determining and optionally quantifying the pattern of RNA expression in a second tissue or cell sample subject to the physiological or pathological change by performing steps (a)-(d) of M1 with the second sample;
- (c) digesting the restriction fragments obtained in step (b) with one or more further restriction endonucleases producing restriction fragments with single-stranded overhangs different from those produced in step (b); and
- (d) comparing the first and the second displays to determine the effect of the internal or external factor on the pattern of RNA expression in the tissue;
- (4) a method (M5) for diagnosis of a disease based on detecting a change in the pattern of DNA fragments in a disease tissue or cell sample comprising:
- (a) determining the pattern of DNA fragments in the sample by:
 - (i) digesting a DNA isolated from the tissue or cell with one or more restriction REI;
 - (ii) ligating the restriction fragments produced from (i) having the same overhangs to a series of adapters whose sequences are complementary to the overhangs;
 - (iii) amplifying the restriction fragments; and
 - (iv) displaying the pattern of DNA fragments in the disease tissue or cell sample;
- (b) determining the pattern of DNA fragments in a normal tissue or cell corresponding to the disease tissue by performing steps (a)-(d) of M1 with the normal tissue; and
- (c) comparing the disease and the normal tissue or cell profile of DNA fragments;
- (5) a method (M6) for detecting a change in the pattern of RNA expression in a cell sample in response to an external factor comprising steps (a) to (d) of M4;
- (6) a method (M7) for constructing an expressed sequence tag (EST) library comprising:
- (a) reverse transcribing an mRNA population isolated from a eukaryotic source to provide a polynucleotide population;
 - (b) digesting a double-stranded cDNA library prepared from the mRNA

with one or more RE1;

(c) ligating the restriction fragments produced from (b) having the same overhangs to a series of adapters whose sequences are complementary to the overhangs;

(d) amplifying the restriction fragments; and

(e) ligating the amplified restriction fragments into a suitable cloning vector;

(7) an isolated nucleic acid comprising an oligonucleotide selected from one of the 64 nucleotide sequences defined in the specification; and

(8) a recombinant host cell transformed with a vector comprising cloned polymerase chain reaction (PCR) obtained from M1.

USE - The method is useful for the simultaneous sequence-specific identification, separation and quantitative measurement of polynucleotide fragments in a polynucleotide population. The method is applicable in DNA fingerprinting, differential display of mRNA, mutation and polymorphism identification, drug screening, molecular taxonomy, and diagnosis of diseases such as heart disease, lung disease, kidney disease, neurodegenerative disease, liver disease, a disease of the reproductive system, or cancer.

The isolated nucleic acid molecule comprising an oligonucleotide selected from one of the 64 nucleotide sequences defined in the specification can be used in any of the methods described above (claimed).

ADVANTAGE - The method is rapid, quantitative and it determines the gene expression level without the requirement of sequence information.

L4 ANSWER 5 OF 6 WPIDS COPYRIGHT 2012 THOMSON REUTERS on STN
ACCESSION NUMBER: 2002-048724 [200206] WPIDS
CROSS REFERENCE: 2001-040475; 2001-366407; 2002-617299
DOC. NO. CPI: C2002-013582 [200206]
TITLE: Isolating DNA containing fragments nicked by Escherichia coli methyl-directed mismatch repair system involves using a modified rolling circle amplification procedure which employs DNA polymerase III
DERWENT CLASS: B04; D16
INVENTOR: LASKEN R; WEISSMAN S
PATENT ASSIGNEE: (LASK-I) LASKEN R; (WEIS-I) WEISSMAN S
COUNTRY COUNT: 1

PATENT INFO ABBR.:

| PATENT NO | KIND DATE | WEEK | LA | PG | MAIN IPC | |
|----------------|-----------------------|------|-------|----|----------|-----|
| US 20010039039 | A1 20011108 (200206)* | EN | 19[5] | | | <-- |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|----------------|----------------|-----------------|----------|
| US 20010039039 | A1 Provisional | US 1998-100996P | 19980918 |
| US 20010039039 | A1 Div Ex | US 1999-398216 | 19990917 |
| US 20010039039 | A1 | US 2001-820356 | 20010329 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|-----------------------|----------------------|--------------|
| US 20010039039 | A1 Div ex | US 6235502 B |
| PRIORITY APPLN. INFO: | US 2001-820356 | 20010329 |
| | US 1998-100996P | 19980918 |
| | US 1999-398216 | 19990917 |
| AN | 2002-048724 [200206] | WPIDS |

CR 2001-040475; 2001-366407; 2002-617299
AB US 20010039039 A1 UPAB; 20060118

NOVELTY - Mismatched DNA containing fragments nicked by MutSLH from two DNA samples are isolated by a modified rolling circle amplification (RCA) method. DNA sample is digested with restriction enzyme, the fragments are ligated to Y-shaped adapters forming adapter-fragment constructs which are nicked by MutSLH proteins and nicked fragments are treated with DNA polymerase(s) which elongates the 3'-OH end.

DETAILED DESCRIPTION - Isolating (M1) mismatched DNA containing fragments nicked by MutSLH (a combination of the three proteins of the Escherichia coli methyl-directed mismatch repair system, collectively called MutSLH) from two DNA samples, comprises:

- (a) digesting a first DNA sample with a restriction enzyme to obtain DNA fragments;
- (b) ligating Y-shaped adapters to the fragments to obtain fragment-plus-adapter constructs;
- (c) repeating the above steps with a second sample;
- (d) methylating the products formed from (c) of the first sample but not the second sample;
- (e) mixing the methylated and unmethylated products obtained from the samples, denaturing and reannealing to form hemimethylated heterohybrids;
- (f) treating the fragments produced in step (e) with a MutSLH preparation to nick DNA containing mismatches and form a 3'-OH end; and
- (g) elongating the 3'-OH end with one or more DNA polymerases.

The method can also be carried out by ligating adapters to DNA fragments to obtain fragment-adapter constructs that have a single-stranded (ss) overhang on the 5'-ends and recessed 3'-ends, where the adapters are blocked with a dideoxynucleotide or other modification that prevents the elongation by a DNA polymerase, carrying out (c)-(e) as above, blocking pre-existing nicks on the fragments with dideoxynucleoside triphosphates or their analogs, treating the fragments with MutSLH preparation to form 3'-OH ends and elongating the ends with a DNA polymerase having strand displacement or nick translation capacity.

INDEPENDENT CLAIMS are also included for the following:

(1) amplifying (M2) DNA using RCA in a manner that results in approximately equimolar amplification of the DNA, by amplifying a circle DNA molecule which comprises a stem-and-loop, or circle DNA molecule containing a universal base, an abasic residue, or other residue that alters the rate of circle replication, where elongation of the circle by a replicating polymerase carrying out the amplification is inhibited;

(2) a method (M3) for using RCA to obtain approximately equimolar amplification of DNA fragment mixtures by introducing at least one pause site in a DNA circle, comprises: (a) placing within the circle a stretch of one or more abasic sites, a region of high secondary structure and a ligand binding site, and then carrying out RCA under conditions such that the pause site slows the DNA polymerase replicating the circle and tends to equalize the number of times the polymerase copies circles of different length; (b) circularizing dsDNA fragments around an adapter such that one strand of the adapter has an internal pause and the outer strand is blocked from ligation at one or both ends; or (c) using a splint that has an internal double stranded (ds) segment containing a pause site on one DNA strand, and which has single stranded extensions at both ends complementary to the ends of the single-stranded fragment to be amplified;

(3) a method (M4) in which fragments of DNA may be circularized and amplified, by cutting DNA with a restriction enzyme that produces a single fragment containing all the markers of the region having pause to be determined, or using the RecA-assisted restriction endonuclease (RARE) method or its variants to produce such a fragment, ligating the cut DNA around an adapter and amplifying the fragment using RCA to obtain a ssDNA from the desired fragment;

(4) amplifying (M5) segments of a DNA target by RCA, by annealing a

padlock DNA that creates a gap comprising the sequence to be amplified, extending the 3'-OH of the padlock DNA with a DNA polymerase which generates a nick, ligating the nick to form a circle DNA, annealing an RCA primer to the circle DNA and carrying out RCA with DNA polymerase III;

(5) a method (M6) in which large fragments of DNA may be circularized and amplified, by providing a DNA-adapter construct which has a DNA fragment ligated around an adapter that has an internal gap and 5' region of non-complementarity and amplifying the DNA-adapter construct using DNA pol III in a RCA;

(6) ligating (M7) adapters onto ends of DNA fragments for use in RCA of the DNA, by ligating restriction endonuclease fragments with an oligonucleotide adapter that forms a hairpin structure with itself such that 3' and 5' ends of the adapter are annealed together and form a proper overhang or blunt end for ligation to the restriction endonuclease fragments, where a circular construct is formed, annealing an oligonucleotide primer to the single-stranded loop portion of the adapters and extending the oligonucleotide primer with a DNA polymerase in RCA reaction; and

(7) carrying out RCA reaction, where at least two different DNA polymerases are employed, one or more of which contains a 3' to 5' exonuclease activity capable of correcting nucleotide misincorporations.

USE - (M1) is useful for isolating mismatched DNA containing fragments nicked by MutS_H from two DNA samples. The procedure allows for the MutS_H nicking of DNA fragments containing mismatched bases to analyze polymorphism between DNA samples. The methods are useful in phase determination, polymorphism analyses, mismatch scanning procedures and cloning procedures, diagnostics (claimed), genotyping, genomic mapping, DNA sequencing and synthesis of DNA probes.

ADVANTAGE - DNA polymerase III holoenzyme provides a superior rate of DNA synthesis and also high processivity which allows rapid replication through regions of high GC content, hair-pin structures, and other regions of secondary structure and regions that normally slow replication due to local sequence context effects.

DESCRIPTION OF DRAWINGS - The figure shows the fragment plus adapter constructs obtained by ligating adapters to DNA fragments, in the amplification of specific DNA sequences by rolling circle amplification.

L4 ANSWER 6 OF 6 WPIDS COPYRIGHT 2012 THOMSON REUTERS on STN
ACCESSION NUMBER: 1997-132667 [199712] WPIDS
DOC. NO. CPI: C1997-042908 [199712]
TITLE: Production, and opt. amplification, of hairpin nucleic acid using a single primer - that is extended to form a template for synthesis of extension product, useful e.g. in gene walking and sequencing
DERWENT CLASS: B04; D16
INVENTOR: DEWHIRST F E
PATENT ASSIGNEE: (FORS-N) FORSYTH DENTAL INFIRMARY FOR CHILDREN
COUNTRY COUNT: 19

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC | |
|------------|------|----------|-----------|----|--------|----------|-----|
| WO 9704131 | A1 | 19970206 | (199712)* | EN | 66[17] | | <-- |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|------------|------|-----------------|----------|
| WO 9704131 | A1 | WO 1996-US11948 | 19960718 |

PRIORITY APPLN. INFO: US 1995-505094
AN 1997-132667 [199712] WPIDS
AB WO 1997004131 A1 UPAB: 20060112

19950721

Production of at least one copy of a hairpin polynucleotide (I) comprises:
(a) combining (I) with a template-dependent polynucleotide polymerase (II); nucleoside triphosphates (NTPs) and excess of one primer (P) that hybridises to a site in the 3' part of (I) and can produce an extension product (EP); (b) dissociating the 2 complementary segments of (I) and (c) allowing hybridisation of P and thus its extension to produce a complementary copy of (I) as an EP.Opt. the process is repeated for amplification.

Also new are kits for the process containing hairpin DNA (the adapter) with a phosphorylated 5' end and ligatable to a blunt or restriction end of double stranded (ds) DNA, plus a ligase, the kits also may contain a polymerase and restriction enzymes.

USE - The method is specified for (1) detecting (I) (from the amplification product) and (2) sequencing ds DNA after its conversion to (I). Typical applications are in gene or chromosome walking; amplification and sequencing of cDNA and detecting even minute amounts of DNA.

ADVANTAGE - Since only a single primer is required, the method allows amplification of flanking regions.

```
=> log
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:hold
COST IN U.S. DOLLARS          SINCE FILE      TOTAL
                               ENTRY        SESSION
FULL ESTIMATED COST          161.58         161.82
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE      TOTAL
                                              ENTRY        SESSION
CA SUBSCRIBER PRICE           -0.87         -0.87
```

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 16:40:33 ON 04 JAN 2012